REMARKS

Claims 1-3, 7 and 11-15 are pending in the instant application. New claim 16 has been added. Support for this claim is provided in the specification at page 17, lines 26-27.

Claims 1-3, 7 and 11-15 have been rejected. Reconsideration is respectfully requested in light of the following remarks and the Supplemental Declaration by Dr. Tsuruda submitted on September 30, 2010. Entry of this Supplemental Declaration into the record and consideration thereof is respectfully requested in light of the Request for Continued Examination filed herewith.

Rejections of Claims 1-3, 7 and 11-15 under 35 U.S.C 103(a)

Claims 1-3, 7 and 11-15 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Tsuruda et al. (WO 01/68061 in view of Honda (U.S. Patent 5,637,293).

Claims 1-3, 7 and 11-15 have also been rejected under 35 U.S.C. 103(a) as being unpatentable over Tsuruda et al. (WO 01/68061) in view of Yasukochi et al. (U.S. Patent Application Publication No. 2005/0053646).

Claims 1-3, 7 and 11-15 have also been rejected under 35 U.S.C. 103(a) as being unpatentable over US 2003/0109819 (hereinafter '819) in view of Tateishi (WO 03/037393).

Applicants respectfully traverse these rejections.

Claim 1 is drawn to a patch preparation comprising a support and an adhesive base, the adhesive base containing 8 to 50 mass % relative to total amount of the adhesive base of a rubber-system macromolecule having a double bond at least in a principal chain thereof and 0.1 to 10 mass % relative to entire amount of the preparation of a nonsteroidal anti-inflammatory analgesic drug, and the adhesive base further containing 0.5 to 20 mass % relative to entire amount of the preparation of 4-tert-butyl-4'-methoxydibenzoylmethane as a stabilizer for the rubber-system macromolecule.

MPEP 2143.01 is clear; the mere fact that references can be combined or modified does not render the resultant combination obvious unless **>the results would have been predictable to one of ordinary skill in the art. *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, ___, 82 USPQ2d 1385, 1396 (2007).

A Declaration by Dr. Tsuruda submitted by Applicant's with the previous response filed March 15, 2010 in the instant patent application demonstrating unpredicted and/or unexpected advantages of a composition comprising 4-tert-butyl-4'-methoxydibenzoylmethane as compared to a

composition comprising the hydroxybenzotriazole derivative Mexoryl® XL was suggested by the Examiner to be unpersuasive because it did not sufficiently compare the instant invention to the closest prior art. Further, the Examiner suggested that because the identity of the hydroxybenzotriazole derivative was not disclosed in the declaration, no proper comparison could be made to what is taught by the prior art. In addition, the Examiner states that "given that these compounds belong to different classes of UV absorbents (e.g. dibenzoylmethane and hydrozybenzotriazole) it is not surprising (i.e. it is completely expected) that there may be differences in their behavior and efficiency."

Accordingly, in an earnest effort to advance the prosecution of this case, Applicants are submitting herewith a Request for Continued Examination with the requisite fee so that consideration is given to the supplemental Declaration by co-inventor Dr. Tsuruda submitted on September 30, 2010. This supplemental Declaration evidences more clearly the unpredicted and/or unexpected advantages of a composition comprising 4-tert-butyl-4'-methoxydibenzoylmethane as compared to a composition comprising the hydroxybenzotriazole derivative Mexoryl® XL.

Applicants respectfully direct the Examiner to paragraphs 3 and 4 of Dr. Tsuruda's Declaration submitted September 30, 2010 wherein experiments comparing the effects of compositions containing ketoprofen and different UV blockers on ear swelling are described. As discussed in paragraph 3 of Dr. Tsuruda's Declaration submitted September 30, 2010, ear swelling is one of the side effects caused by decomposition products (i.e. radicals) of nonsteroidal antiinflammatory drugs (NSAIDs). In the comparative experiments performed, ethanol solutions containing 2% of the NSAID ketoprofen and either 3% 4-tert-butyl-4'-methoxydibenzoylmethane (BM-DBM), or no UV blocker (referred to as controls) were applied to the ear of Balb/c mice (female, 9-11 weeks of age), followed by irradiation of 40 J/cm^2 of UVA (see paragraph 3 of Dr. Tsuruda's Declaration submitted September 30, 2010). The IUPAC name 2-(2H-benzotriazol-2-yl)-4-methyl-6-[2-methyl-3-[1,3,3,3-tetramethyl-1-(trimethylsilyl)oxy] disiloxanyl]propyl] phenol) for Mexoryl® XL is also provided in paragraph 3 of Dr. Tsuruda's Declaration submitted September 30, 2010.

Results comparing measured thicknesses of the ears after 24 hours irradiation are shown in Figure 1 attached to Dr. Tsuruda's Declaration submitted September 30, 2010. As

shown by Figure 1 and discussed in paragraph 4 of Dr. Tsuruda's Declaration submitted September 30, 2010, while both solutions containing UV blockers suppressed the increase in ear thickness indicative of swelling as compared to solutions containing no UV blocker (controls), 3% BM-DBM reduced ear swelling by about 55% compared to the controls while 3% Mexoryl® XL reduced ear swelling by only about 20% compared to the controls. Accordingly, BM-DBM was 2.75 times more effective at preventing photodecomposition of the NSAID ketoprofen to its radical form than the benzotriazole derivative Mexoryl® XL. See Figure 1 and paragraph 4 of Dr. Tsuruda's Declaration submitted September 30, 2010. From these experiments, Dr. Tsuruda states in paragraph 4 that BM-DBM "is expected to be a significantly better stabilizer of the rubber system macromolecule than the benzotriazole derivative Mexoryl® XL."

MPEP 716.02(a) and the case law state "A greater than expected result is an evidentiary factor pertinent to the legal conclusion of obviousness ... of the claims at issue." *In re Corkill*, 711 F.2d 1496, 226 USPQ 1005 (Fed. Cir. 1985).

MPEP 716.02(a) and the case law also state "Applicants must further show that the results were greater than those

which would have been expected from the prior art to an unobvious extent, and that the results are of a significant, practical advantage." *Ex parte The NutraSweet Co.*, 19 USPQ2d 1586 (Bd. Pat. App. & Inter. 1991).

A 2.75 fold increase in efficacy of a composition comprising BM-DBM at preventing photodecomposition of the NSAID ketoprofen to its radical form as compared to the benzotriazole derivative Mexoryl® XL as shown by Figure 1 and discussed in paragraph 4 of Dr. Tsuruda's Declaration submitted September 30, 2010 is clearly a greater than expected result over cited teachings of Tsuruda et al. (WO 01/68061), US 2003/0109819, Yasukochi et al. (U.S. Patent Application Publication No. 2005/0053646) and Tateishi (WO 03/037393), none of which actually teach use of BM-DMA. A 2.75 fold increase in efficacy of a composition comprising BM-DBM is also a clearly greater than expected result over Honda (U.S. Patent 5,637,293), which teaches BM-DBM to act equivalently to other UV blockers tested (see Tables 1 and 2 of Honda). Further, there is a practical, significant advantage of these results, specifically that BM-DBM is expected to be a significantly better stabilizer of the rubber system macromolecule than the benzotriazole

derivative Mexoryl® XL. See paragraph 4 of Dr. Tsuruda's Declaration submitted September 30, 2010.

MPEP 716.02(a) further states "Evidence of unobvious or unexpected advantageous properties, such as superiority in a property the claimed compound shares with the prior art, can rebut *prima facie* obviousness. Evidence that a compound is unexpectedly superior in one of a spectrum of common properties . . . can be enough to rebut a *prima facie* case of obviousness." Thus, the fact that BM-DBM and Mexoryl® XL are both UV blockers does not diminish this evidence of unobviousness based upon demonstrated clear superiority of BM-DBM in accordance with the instant claimed invention.

Also provided with Dr. Tsuruda's Declaration submitted September 30, 2010 are absorption curves from two publicly available documents relating to the UV blockers Mexoryl® XL and avobenzone (also known as BM-DBM) and 2-(2-hydroxy-5-methylphenyl) benzotriazole. See paragraph 5 of Dr. Tsuruda's Declaration submitted September 30, 2010. According to these curves, Mexoryl® XL and 2-(2-hydroxy-5-methylphenyl)benzotriazole have similar absorption curves. Accordingly, the experiments presented in both of Dr. Tsuruda's Declaration are predictive of how other benzotriazole derivatives such as the UV blocker 2-(2-

hydroxy-5-methylphenyl)benzotriazole disclosed by Honda, as well as Tsuruda et al. (WO 01/68061), US 2003/0109819, would perform. See paragraph 5 of Dr. Tsuruda's Declaration submitted September 30, 2010. Thus, these experiments meet the requirements of MPEP 716.02(e) that the affidavit or declaration under 37 CFR 1.132 compare the claimed subject matter with the closest prior art, thereby effectively rebutting any *prima facie* case of obviousness. Also see *In re Burckel*, 592 F.2d 1175, 201 USPQ 67 (CCPA 1979). Applicants have appropriately compared the claimed UV blocker BM-DBM with a UV blocker Mexoryl® XL that is equally closely related to the UV blocker 2-(2-hydroxy-5-methylphenyl)benzotriazole disclosed in the prior art of Tsuruda et al. (WO 01/68061) and US 2003/0109819 and taught to be equivalent to BM-DBM by Honda. See *In re Holladay*, 584 F.2d 384, 199 USPQ 516 (CCPA 1978).

MPEP 716.02(e) is clear; an applicant does not have to test all the compounds taught by each reference. Comparative data presented in Dr. Tsuruda's Declaration submitted September 30, 2010 clearly meets the requirements of MPEP 716.02(e), however, that where an applicant tests less than all cited compounds, *the test must be sufficient to permit a conclusion respecting the relative effectiveness*

of applicant's claimed compounds and the compounds of the closest prior art." Id. (quoting *In re Payne*, 606 F.2d 303, 316, 203 USPQ 245, 256 (CCPA 1979)) (emphasis in original).).

Also shown by the absorption curves provided with Dr. Tsuruda's Declaration submitted September 30, 2010 is that the best effective absorption wavelength of avobenzone is longer than that of the two benzotriazole derivatives. Thus, contrary to the Examiner's assertion, avobenzone (BM-DBM) would not necessarily be expected by a skilled artisan to function in the same manner as Mexoryl® XL and 2-(2-hydroxy-4-methylphenyl)benzotriazole in transdermal patches based upon their differing absorption curves. See paragraph 5 of Dr. Tsuruda's Declaration submitted September 30, 2010. Clearly in no way would the claimed UV blocker BM-DBM be expected to function so much more effectively, specifically, 2.75 times more effectively, than the benzotriazole derivatives disclosed by cited references of Tsuruda et al. (WO 01/68061) and US 2003/0109819 and taught to be equivalent to BM-DBM by Honda.

The evidence submitted via the supplemental Declaration submitted September 30, 2010 of superior and unexpected properties of the instant claimed invention rebuts any prima

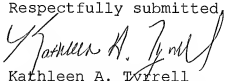
facie of obviousness over the cited combinations of references. See MPEP 2145.

Withdrawal of these rejections under 35 U.S.C. 103 is respectfully requested.

Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,



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